NEWS IPC8

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FILE 'HOME' ENTERED AT 16:04:58 ON 16 MAY 2008

=> file medline

COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 0.21 0.21

FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 16:05:18 ON 16 MAY 2008

FILE LAST UPDATED: 15 May 2008 (20080515/UP). FILE COVERS 1949 TO DATE.

MEDLINE has been updated with the National Library of Medicine's revised 2008 MeSH terms. See HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

See HELP RANGE before carrying out any RANGE search.

=> s (three hybrid system and methasone-FK506)

1321800 THREE

66747 HYBRID

1392301 SYSTEM

102 THREE HYBRID SYSTEM

(THREE (W) HYBRID (W) SYSTEM)

133 METHASONE

3830 FK506

0 METHASONE-FK506

(METHASONE (W) FK506)

L1 0 (THREE HYBRID SYSTEM AND METHASONE-FK506)

=> s FK506

L2 3830 FK506

=> s 12 and (methotrexate)

33516 METHOTREXATE

L3 70 L2 AND (METHOTREXATE)

=> s 13 and ligand

127155 LIGAND

L4 2 L3 AND LIGAND

=> d 14 ti abs ibib tot

L4 ANSWER 1 OF 2 MEDLINE on STN

TI Immunopathogenesis of acute graft-versus-host disease: implications for novel preventive and therapeutic strategies.

AB Acute graft-versus-host disease (GVHD) is a primary T-cell-mediated complication of allogeneic hematopoietic stem cell transplantation (HSCT), occurring when donor-derived T cells are stimulated by host antigen-presenting cells (APCs), enhanced by proinflammatory cytokines such as interleukin (IL)-1, IL-6, IL-8, and tumor necrosis factor (TNF)-alpha. Recent data indicate that besides differences in major histocompatibility and minor histocompatibility antigens, cytokine gene polymorphisms have a predictive value for the complication of GVHD. Patients with a high anti-inflammatory IL-10 production have been demonstrated to be protected from GVHD while patients with high TNF-alpha

serum levels were more at risk for GVHD. Pharmacological immunosuppression for GVHD prophylaxis and therapy, including unspecific approaches with corticosteroids or methotrexate (MTX), as well as more specific therapy with cyclosporin A (CsA), tacrolimus ( FK506), sirolimus, mycophenolate mofetil (MMF), antithymocyte globulin (ATG), and monoclonal antibodies (MAbs) directed against CD3, CD25, CD52, cytotoxic T-lymphocyte antigen (CTLA)-4, CD40 ligand , or TNF-alpha, have been proven to be effective. Recent data on novel techniques to selectively deplete alloreactive T cells by removal, destruction, or anergy induction while preserving leukemia-specific T-cell clones suggest a clinical benefit from these approaches. Gene-modified T cells that can selectively be depleted and CD4(+)CD25(+) regulatory T cells are under investigation for their ability to modulate alloreactivity after HSCT. With a better understanding of the immunopathogenesis of acute GVHD and the technical improvement of recently described therapeutic approaches, such as removal of naive T cells, selection of Th2 cells, suicide gene transduced T cells, and adoptive transfer of regulatory T cells, the use of alloreactivity as a treatment modality may be expanded to nonhematological disease entities such as solid tumors or autoimmune disorders.

ACCESSION NUMBER: 2004478960 MEDLINE DOCUMENT NUMBER: PubMed ID: 15449032

TITLE: Immunopathogenesis of acute graft-versus-host disease:

implications for novel preventive and therapeutic

strategies.

AUTHOR: Zeiser Robert; Marks Reinhard; Bertz Hartmut; Finke Jurgen

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SOURCE: Annals of hematology, (2004 Sep) Vol. 83, No. 9, pp.

551-65. Electronic Publication: 2004-06-15. Ref: 183

Journal code: 9107334. ISSN: 0939-5555. Germany: Germany, Federal Republic of

PUB. COUNTRY: Germany: Germany, Federal Republic on DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200410

ENTRY DATE: Entered STN: 28 Sep 2004

Last Updated on STN: 22 Oct 2004 Entered Medline: 20 Oct 2004

- L4 ANSWER 2 OF 2 MEDLINE on STN
- TI Correlation between ligand-receptor affinity and the transcription readout in a yeast three-hybrid system.
- The yeast two-hybrid assay has proven to be a powerful method to detect AΒ protein-protein interactions as well as to derive genome-wide protein interaction maps. More recently, three-hybrid assays have emerged as a means to detect both protein-RNA and protein-small molecule interactions. Despite the routine use of the two-hybrid assay and the potential of three-hybrid systems, there has been little quantitative characterization to understand how the strength of the protein interaction correlates with transcription activation. It is not known if the additional interaction in three-hybrid systems compromises the sensitivity of the system. Thus, here, we set out to determine the K(D) cutoff of a small molecule three-hybrid system and to determine if there is a correlation between the K(D) and the levels of transcription activation. A series of mutations to FK506-binding protein 12 (FKBP12) were designed to vary the affinity of this protein for the small molecule synthetic ligand for FK506-binding protein 12 (SLF). These FKBP12 variants were overexpressed and purified, and their K(D)'s for SLF were measured using a

fluorescence polarization assay. Then the levels of transcription activation in a Mtx-DHFR yeast three-hybrid system were determined for these variants using a lacZ reporter gene. The K(D) cutoff of the Mtx yeast three-hybrid system is found to be ca. 50 nM. Further, the levels of transcription activation correlate with the strength of the binding interaction, though the dynamic range is only 1 order of magnitude. These results establish that the three-hybrid assay has the requisite sensitivity for drug discovery. However, the small dynamic range highlights a limitation to equilibrium-based assays for discriminating interactions based on affinity.

ACCESSION NUMBER: 2004397997 MEDLINE DOCUMENT NUMBER: PubMed ID: 15301533

TITLE: Correlation between ligand-receptor affinity and

the transcription readout in a yeast three-hybrid system. AUTHOR: de Felipe Karim Suwwan; Carter Brian T; Althoff Eric A;

Cornish Virginia W

CORPORATE SOURCE: Integrated Program in Cellular, Molecular, and Biophysical

Studies, Columbia University, New York, New York 10027,

USA.

CONTRACT NUMBER: R01-GM62867 (United States NIGMS)

SOURCE: Biochemistry, (2004 Aug 17) Vol. 43, No. 32, pp. 10353-63.

Journal code: 0370623. ISSN: 0006-2960.

PUB. COUNTRY: United States

DOCUMENT TYPE: (COMPARATIVE STUDY)

Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200409

ENTRY DATE: Entered STN: 11 Aug 2004

Last Updated on STN: 15 Sep 2004 Entered Medline: 14 Sep 2004

=> d his

L1

(FILE 'HOME' ENTERED AT 16:04:58 ON 16 MAY 2008)

FILE 'MEDLINE' ENTERED AT 16:05:18 ON 16 MAY 2008

0 S (THREE HYBRID SYSTEM AND METHASONE-FK506)

L2 3830 S FK506

L3 70 S L2 AND (METHOTREXATE)

L4 2 S L3 AND LIGAND

=> s (enzyme cleavable linker) and (dimerize protein)

714136 ENZYME

2512 CLEAVABLE

12299 LINKER

1 ENZYME CLEAVABLE LINKER

(ENZYME (W) CLEAVABLE (W) LINKER)

1147 DIMERIZE

1792807 PROTEIN

0 DIMERIZE PROTEIN

(DIMERIZE (W) PROTEIN)

L5 0 (ENZYME CLEAVABLE LINKER) AND (DIMERIZE PROTEIN)